Pupil changes during cardiopulmonary bypass

G. C. Fletcher, A. J. Asbury and J. H. Brown

Summary
Pupil diameter is used during anaesthesia to assess depth of anaesthesia and indicate cerebral hypoxia. This is especially so during cardiac bypass when other autonomic signs cannot be monitored. We have used a pupillometer to determine the effect of cardiopulmonary bypass on the pupil. We have also investigated if any effect was caused by washout of opioid from the central nervous system by allocating patients to one of two groups: in one the bypass pump was preloaded with fentanyl, in the other with 0.9 % saline. Cardiopulmonary bypass caused pupil dilatation of between 17 % and 53 %, which was unaffected by preloading the bypass pump with fentanyl. This effect lasted for the duration of the study, which ended 30 min after the start of cardiopulmonary bypass. Sym pathetic nervous system reflexes and hypothermia may account for this observation, but further research is necessary to exclude other contributory factors. (Br. J. Anaesth. 1996; 76: 20–22)

Key words

Cardiac anaesthetists are likely to inspect the pupils at several stages during operation and especially during the bypass phase. Subjective assessment of pupil size has been used as one component to estimate depth of anaesthesia [1]. Increasing concern regarding postoperative morbidity is now evident [2, 3] and has focused attention on possible predictive factors, such as alterations in pupil diameter and reactivity [4].

There are few publications on the effect of cardiopulmonary bypass (CPB) on the eye. One of these has described a surprising increase in intraocular pressure (IOP) [5]. The pupillary response to the commencement of CPB has never been documented.

Many physiological and pharmacological factors affect pupil diameter [6, 7], including opioids, anticholinergics, ganglion blockers, sympathomimetics, histamine and steroids. However, the sudden change in so many variables which occurs on starting CPB makes speculation on the resulting pupillary changes unproductive.

A recently developed pupillometer [8] which is robust, easy to use and accurate (0.1 mm) now permits pupillary changes, perhaps previously undetected, to be observed. The aim of this study was twofold: first, to record pupil changes which occur when patients undergo CPB. It was postulated that any change in pupil diameter may be the result of a washout effect of the bypass prime solution on the opioid in the Edinger–Westphal nucleus. Therefore, our second aim was to determine if preloading the bypass pump with fentanyl affected the observed pupil changes.

Patients and methods

Local hospital Ethics Committee approval was obtained and informed consent was given by all participating patients.

Observations of pupil size were carried out in 20 patients, aged 44–69 yr. Eye colour was noted as this has been shown to affect pupil reactivity. Patients were premedicated with lorazepam 2–3 mg the night before and 2–3 mg on the morning of operation. The anaesthetic technique was similar in all patients. Anaesthesia was induced with fentanyl 5 μg kg⁻¹ i.v. and propofol, delivered from a target-controlled infusion pump set to infuse to a target of 1–3 μg ml⁻¹ [9]. All patients were given pancuronium 0.2 mg kg⁻¹ and anaesthesia was maintained with an infusion of fentanyl of 10 μg kg⁻¹ h⁻¹ (to a total of 30 μg kg⁻¹) and a target-controlled propofol infusion [9]. The lungs were ventilated with an air–oxygen mix (FiO₂ of 0.4). Arterial pressures and central venous pressures were monitored by invasive techniques. A further bolus of fentanyl 5 μg kg⁻¹ was given just before incision.

In all cases the extracorporeal circulation involved a Cobe CMS, flat sheet membrane oxygenator primed with Hartmann’s solution 2000 ml, heparin 8000 u., potassium chloride 15 mmol, sodium bicarbonate 50 mmol, mannitol 10 g and cefuroxime 750 mg. Patients were allocated randomly into one of two groups using opaque envelopes (saline or fentanyl). In group F, fentanyl 5 μg kg⁻¹ was injected into the reservoir of the pump before bypass, in the NonF group, an equivalent volume of normal saline was given into the reservoir. The patients were unaware of the group into which they were placed as was the researcher who measured pupil diameter. The cardioplegic solution (St Thomas’ solution 700–1000 ml) was given to cause asystole. During

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bypass methoxamine i.v. was given to maintain mean arterial pressure greater than 40 mm Hg. At the surgeons' request, 16 patients were cooled to a temperature of 28 °C and four were cooled to 30 °C.

Pre-bypass pupil diameter was recorded during the last minutes before commencing CPB. Readings were then recorded at 30 s, and at 1, 3, 5, 10, 15, 20 and 30 min thereafter.

The Mann–Whitney U test in Minitab version 9.2 was used to assess statistical significance between the independent groups and the Wilcoxon signed rank sum test was used for intra-group comparison. Significance was taken at $P < 0.05$.

**Results**

There were 17 males and three females in the study. Of these patients, 18 were undergoing coronary artery bypass graft, one mitral valve repair and one aortic valve repair. None of the patients had an eye disease other than being long-sighted.

The ages of the patients in the two groups (F and NonF) were not significantly different ($P < 0.05$). Median age in group F was 59 (interquartile range 51.75–65.25) yr and in group NonF 59 (53.75–63.75) yr. Thirteen patients had blue eyes, three brown, two green and two grey. The time to commencement of CPB varied between 50 and 140 min.

There was a significant increase in pupil diameter ($P < 0.001$) compared with pre-bypass size at all times of measurement after the start of CPB (fig. 1). The time of maximum pupil dilatation was 5 min when median dilatation was 0.4 mm (interquartile range 0.3–0.5 mm). Maximum pupil size observed in any one patient was 0.9 mm and the minimum was 0.3 mm. The magnitude of the observed increase in pupil diameter during CPB was not significantly affected by preloading the bypass pump with fentanyl (fig. 2). The population size was too small to make inferences about the effect of eye colour, although the mean pre-bypass diameter and the mean maximum change in diameter for each eye colour is shown in table 1.

One patient developed bilateral conjunctivitis after operation which was considered to be unlikely to be related to the study as only one eye was used for pupil measurements, and nothing came into contact with the surface of the eye.

**Discussion**

During general anaesthesia there are variations in pupil size [6, 7] and these changes tend to be more pronounced when autonomically active drugs, opioids and central nervous system depressants are given. Such effects occur throughout cardiac anaesthesia, but the sustained and reproducible pattern of pupil dilatation which we have observed during CPB is likely to depend on other physiological variables.

Patients in the study received moderate doses of fentanyl and the mean pre-bypass pupil diameter of 1.75 mm correlates with the effects of a bolus dose of fentanyl to an anaesthetized patient, when mean pupil diameter is reduced from approximately 3.0 to 2.0 mm [10]. Opioids are thought to affect the pupil by reducing cortical inhibition of the Edinger–Westphal nucleus. Binding of fentanyl to receptors in this area might be influenced by the sudden change in plasma concentration as the crystalloid prime flushes through the body. However, this is unlikely as the changes in pupil diameter in the group which had the bypass prime solution preloaded with fentanyl did not differ significantly from those in which the pump was preloaded with saline.

Hypothermia itself is known to dilate the pupils [11] and also reduce IOP. This factor may have played a part in causing the observed pupil dilatation. Investigation of patients undergoing normothermic CPB would help to clarify this.

Autonomic effects on the pupil, mediated via the ciliary ganglion, are obvious in conscious people, and in ophthalmic surgery direct effects of topical autonomically active drugs are used to good effect [12]. During CPB, it is likely that there is both a neurotransmitter and a neuroendocrine response caused by emptying of the atria of the heart and a

![Figure 1](image1.png)

**Figure 1** Median (interquartile range) pupil diameter before (Pre) and after commencement of cardiopulmonary bypass.

![Figure 2](image2.png)

**Figure 2** Median (interquartile range) pupil diameter before (Pre) and after commencement of cardiopulmonary bypass in patients whose bypass pump was preloaded with fentanyl (■) or 0.9 % saline (□).

<table>
<thead>
<tr>
<th>Eye colour</th>
<th>No. of patients</th>
<th>Mean pre-bypass pupil diameter (mm)</th>
<th>Mean maximum pupil dilatation (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blue</td>
<td>13</td>
<td>1.76</td>
<td>0.52</td>
</tr>
<tr>
<td>Green</td>
<td>2</td>
<td>1.35</td>
<td>0.45</td>
</tr>
<tr>
<td>Brown</td>
<td>3</td>
<td>1.73</td>
<td>0.43</td>
</tr>
<tr>
<td>Grey</td>
<td>2</td>
<td>2.05</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Table 1 Effect of eye colour on the changes in pupil diameter during CPB.
tendency for a reduction in mean arterial pressure. Measurements of plasma catecholamine concentrations have shown that during CPB plasma noradrenaline concentration increases to a maximum at 60 min and dopamine concentrations increase by 500% at 15 min and then diminish over the next 45 min [13]. In this context it is worth noting the results of Von Sallmann and Lowenstein who used electrode stimulation of the ventral zone of the hypothalamus in cats to mimic the effects of diffuse sympathetic nervous system discharge [14]. They found that IOP increased, but did not comment on any effects on the pupil. It might be expected that a central sympathetic response to the sudden hypotension of CPB would produce much larger increases in pupil diameter than we have observed. Also, the corresponding increase in IOP described by Stellpflug and colleagues [5] was of only a moderate degree. An explanation may be that pupil reactivity is attenuated by the central opioid effect, and hypotension, while triggering the sympathetic nervous system to increase IOP, itself tends to lower IOP [15].

Although sympathetic activity provides a likely explanation for the observed increase in pupil diameter associated with CPB, other physiological variables may play a part [16–21]. There was also a source of error in this study as a result of reading the pupillometer.

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References